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L10           3 SEA FILE=HCAPLUS ABB=ON  L9 AND (?BRAIN?(W)(?DAMAGE? OR
                ?DISEAS?) OR ?ISCHEM? OR ?HEMORRH? OR ?INFARCT? OR ?INJUR? OR
                ?SUBARACHNOID? OR ?CEREB?(W)?THROMB? OR ?EMBOLISM? OR ?CARDIAC?
                (W)?ARREST? OR ?STROKE? OR ?TRANSIENT?(W)?ISCHEM?(W)?ATTACK?
                OR TIA)
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L12           1 SEA FILE=HCAPLUS ABB=ON  L9 AND L11
L13           3 SEA FILE=HCAPLUS ABB=ON  L10 OR L12
L14      144354 SEA FILE=HCAPLUS ABB=ON  ISCHEMIA+ALL/CT
L15           3 SEA FILE=HCAPLUS ABB=ON  L9 AND L14
L16           3 SEA FILE=HCAPLUS ABB=ON  L13 OR L15
L23           7 SEA FILE=HCAPLUS ABB=ON  L9 OR L16
L24           3 SEA FILE=HCAPLUS ABB=ON  L23 AND (PRD<19990721 OR PD<19990721)

=> d ibib abs hitstr l24 1-3

L24  ANSWER 1 OF 3  HCAPLUS  COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:         1994:280293  HCAPLUS
DOCUMENT NUMBER:          120:280293
TITLE:                    Pharmaceutical compositions and use of macrolide
                          compounds for the treatment of reversible obstructive
                          airways disease
INVENTOR(S):              Hallam, Catherine; Harper, Stephen Thomas
PATENT ASSIGNEE(S):       Fisons PLC, UK
SOURCE:                   PCT Int. Appl., 22 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.         DATE
     ---------------      ----   --------    --------------------    --------
     WO 9404148            A1    19940303    WO 1993-GB1769          19930820 <--
         W:  AU, CA, JP, KR, NO, NZ
         RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
     ZA 9306137            A     19940221    ZA 1993-6137            19930820 <--
     AU 9349671            A1    19940315    AU 1993-49671           19930820 <--
PRIORITY APPLN. INFO.:                       GB 1992-18027       A   19920825 <--
                                             WO 1993-GB1769      W   19930820 <--
OTHER SOURCE(S):          MARPAT 120:280293
GI
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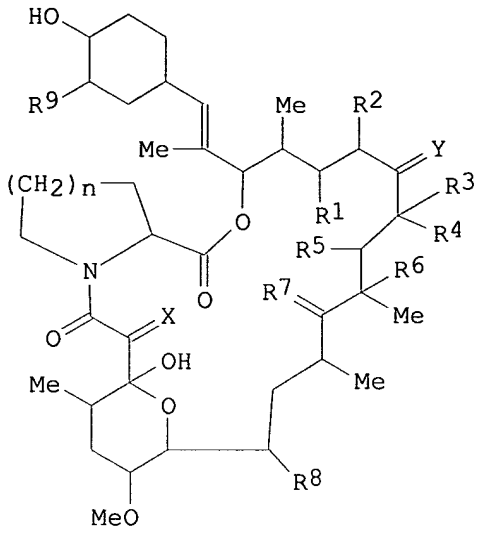


I

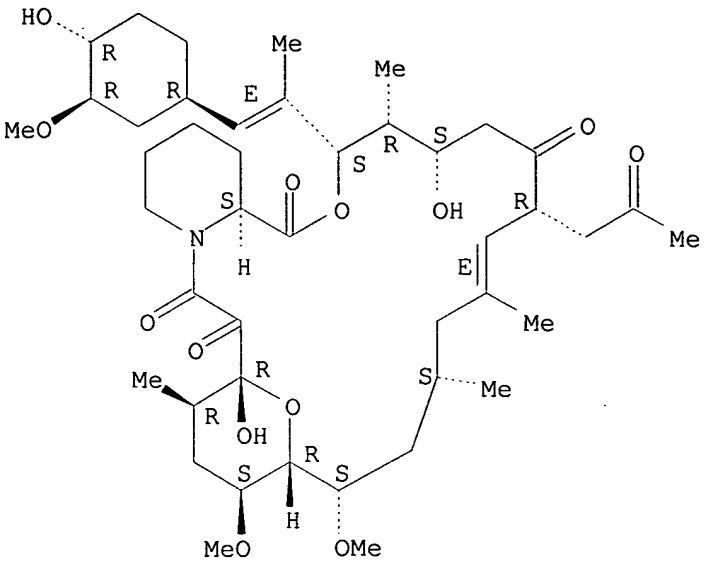
AB The title macrolides I [R1, R2 = H, OH, or may together represent a 2nd C-C bond between the C atoms to which they are attached; R3 = (CO2H-substituted) Me, (O- or OH- or CO2H-substituted) Et, (O- or OH-substituted) Pr, (OH-substituted) allyl; R4 = H; R5 and R6 together represent a 2nd C-C bond between the C atoms to which they are attached; R7 represents O, (H, R7a) (R7a = H, OH); R8, R9 = OH, OCH3; X, Y = O, (H, OH); n = 1,2; in addition to the above, R1 and R5; R7a and R8; and R3, R4 and Y may form various rings together with the C atoms to which they are attached; with certain provisos], and pharmaceutically acceptable derivs. thereof, are used in the manufacture of a medicament for the treatment of reversible obstructive airways diseases. An aerosol formulation of 17-(2-oxopropyl)-1,14-dihydroxy-12-[2-(4-hydroxy-3-methoxycyclohexyl)-1-methylvinyl]-23,25-dimethoxy-13,19,21,27-tetramethyl-11,28-dioxa-4-azatricyclo[22.3.1.04,9]octacos-18-ene-2,3,10,16-tetraone (II) is presented. II was tested in a mast cell screen and was found to inhibit histamine release by 50% of its maximum value at 1 X 10-8 M.

IT **124554-37-6 124554-37-6D**, derivs.
RL: BIOL (Biological study)
(for reversible obstructive airways disease treatment)

RN 124554-37-6 HCAPLUS

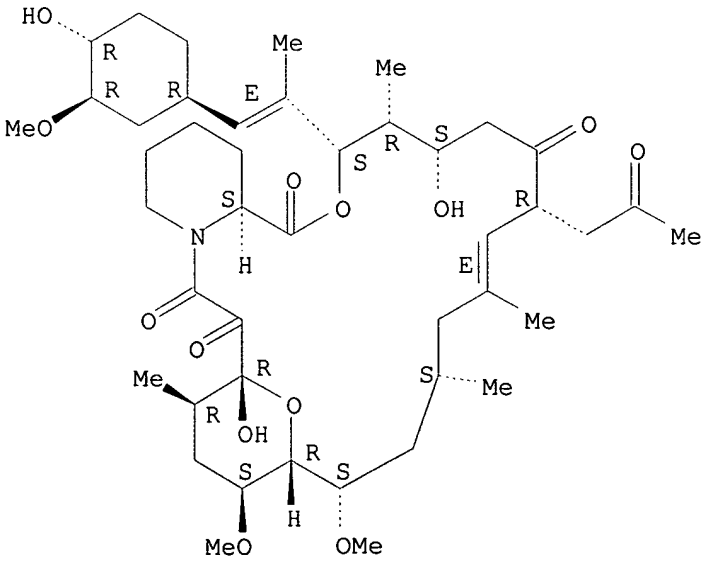
CN 15,19-Epoxy-3H-pyrido[2,1-c][1,4]oxaazacyclotricosine-1,7,20,21(4H,23H)-tetrone, 5,6,8,11,12,13,14,15,16,17,18,19,24,25,26,26a-hexadecahydro-5,19-dihydroxy-3-[(1E)-2-[(1R,3R,4R)-4-hydroxy-3-methoxycyclohexyl]-1-methylethenyl]-14,16-dimethoxy-4,10,12,18-tetramethyl-8-(2-oxopropyl)-, (3S,4R,5S,8R,9E,12S,14S,15R,16S,18R,19R,26aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 124554-37-6 HCAPLUS
CN 15,19-Epoxy-3H-pyrido[2,1-c][1,4]oxaazacyclotricosine-1,7,20,21(4H,23H)-tetrone, 5,6,8,11,12,13,14,15,16,17,18,19,24,25,26,26a-hexadecahydro-5,19-dihydroxy-3-[(1E)-2-[(1R,3R,4R)-4-hydroxy-3-methoxycyclohexyl]-1-methylethenyl]-14,16-dimethoxy-4,10,12,18-tetramethyl-8-(2-oxopropyl)-, (3S,4R,5S,8R,9E,12S,14S,15R,16S,18R,19R,26aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



L24 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1992:6340 HCAPLUS
DOCUMENT NUMBER: 116:6340
TITLE: Preparation of rapamycin analogs for treatment of

immunosuppression

INVENTOR(S): Donald, David Keith; Furber, Mark; Hardern, David Norman; Leff, Paul

PATENT ASSIGNEE(S): Fisons PLC, UK

SOURCE: PCT Int. Appl., 48 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE	
WO 9104025	A1	19910404	WO 1990-GB1412		19900913	<--
W: CA, JP, KR, US						
RW: AT, BE, CH, DE, DK, ES, FR, GB, IT, LU, NL, SE						
CA 2065425	AA	19910315	CA 1990-2065425		19900913	<--
EP 491797	A1	19920701	EP 1990-913838		19900913	<--
R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, LU, NL, SE						
JP 05500215	T2	19930121	JP 1990-512909		19900913	<--
PRIORITY APPLN. INFO.:			GB 1989-20849	A	19890914	<--
			GB 1989-20985	A	19890915	<--
			GB 1990-6449	A	19900322	<--
			GB 1990-12795	A	19900608	<--
			GB 1990-14959	A	19900706	<--
			WO 1990-GB1412	W	19900913	<--

OTHER SOURCE(S): MARPAT 116:6340

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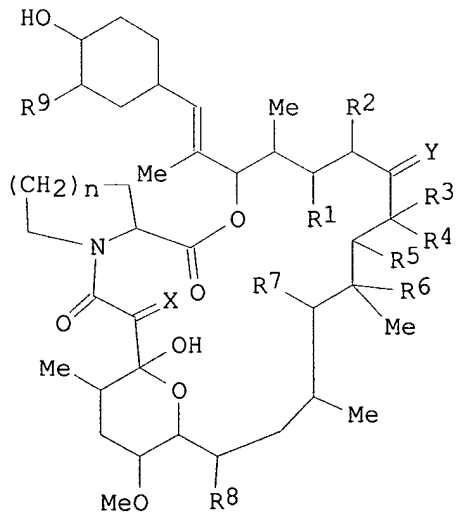
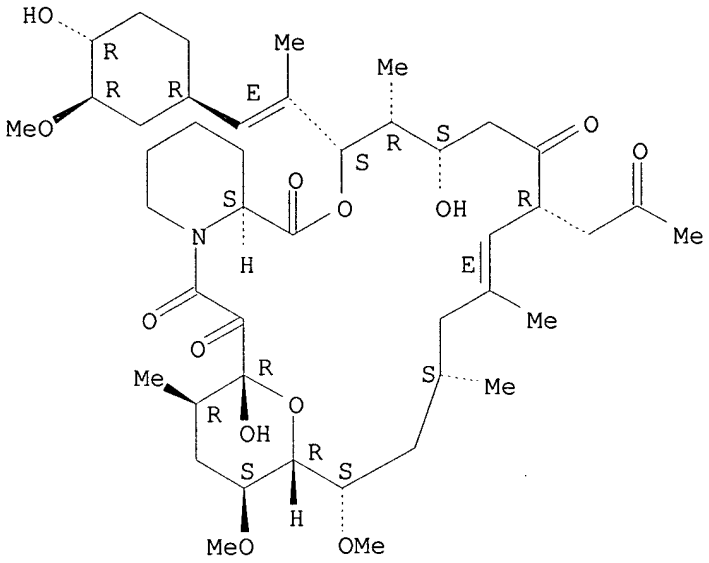


I

AB The title compds. [I; R1,R2,R7 = H, OH; R1R2 = bond; R3 = Me, CH2CH2OH, (un)esterified or (un)amidated (CH2)m CO2H, etc.; R4 = H; R5R6 = bond; R8 = OMe; R9 = OH, OMe; R1R5 = O and R6R7 = bond; R7R8 = O and R3R4Y = atoms to complete a Me-substituted furanyl ring; X, Y = O, (H,OH); m = 1-3; n= 1,2] were prepared Thus, a DMF solution of I (R5R6 = bond, R4 = R7 = H, R8 = R9 = OMe, X = Y = O, n = 2) (II; R1R2 = bond, R3 = CH2CH:CH2) containing PdCl2 and CuCl was oxygenated 3 h and the product hydrogenated over Pd/C to give II (R3 = CH2COMe) (IV; R1 = R2 = H). IV (R1 = OH, R2 = H) had pA2 of 8.3 in the mixed lymphocyte reaction against FR-900506.

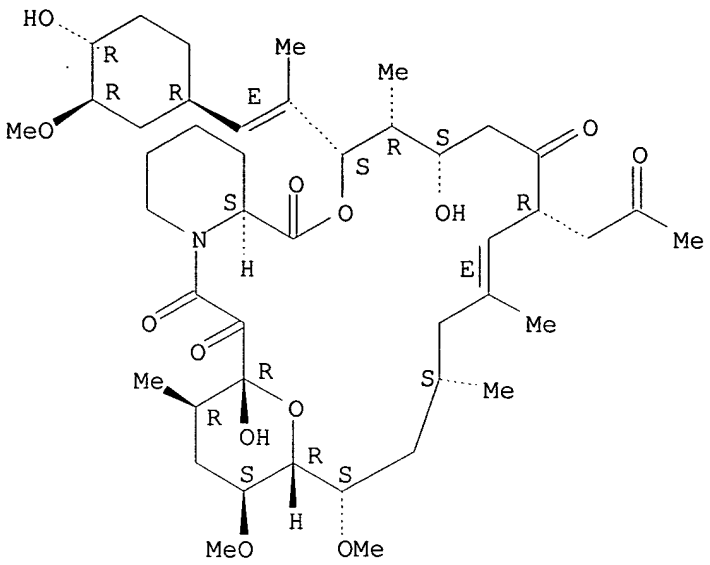
IT **124554-37-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as immunosuppressive antagonist)
RN 124554-37-6 HCAPLUS
CN 15,19-Epoxy-3H-pyrido[2,1-c][1,4]oxaazacyclotricosine-1,7,20,21(4H,23H)-tetrone, 5,6,8,11,12,13,14,15,16,17,18,19,24,25,26,26a-hexadecahydro-5,19-dihydroxy-3-[(1E)-2-[(1R,3R,4R)-4-hydroxy-3-methoxycyclohexyl]-1-methylethenyl]-14,16-dimethoxy-4,10,12,18-tetramethyl-8-(2-oxopropyl)-, (3S,4R,5S,8R,9E,12S,14S,15R,16S,18R,19R,26aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



IT **124554-37-6**
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, in preparation of immunosuppressive antagonists)
RN 124554-37-6 HCAPLUS
CN 15,19-Epoxy-3H-pyrido[2,1-c][1,4]oxaazacyclotricosine-1,7,20,21(4H,23H)-tetrone, 5,6,8,11,12,13,14,15,16,17,18,19,24,25,26,26a-hexadecahydro-5,19-dihydroxy-3-[(1E)-2-[(1R,3R,4R)-4-hydroxy-3-methoxycyclohexyl]-1-methylethenyl]-14,16-dimethoxy-4,10,12,18-tetramethyl-8-(2-oxopropyl)-, (3S,4R,5S,8R,9E,12S,14S,15R,16S,18R,19R,26aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



L24 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1990:458793 HCAPLUS
DOCUMENT NUMBER: 113:58793
TITLE: Preparation of macrolide compounds as immunosuppressants
INVENTOR(S): Cooper, Martin Edward; Donald, David Keith; Hardern, David Norman
PATENT ASSIGNEE(S): Fisons PLC, UK
SOURCE: PCT Int. Appl., 60 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 8905304	A1	19890615	WO 1988-GB1093	19881202 <--
W: AU, DK, FI, HU, JP, KR, NO, US				
RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
AU 8928228	A1	19890705	AU 1989-28228	19881202 <--
AU 630866	B2	19921112		
EP 323042	A1	19890705	EP 1988-311422	19881202 <--
R: ES, GR				
EP 346427	A1	19891220	EP 1989-900628	19881202 <--
EP 346427	B1	19950329		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
JP 02502463	T2	19900809	JP 1989-500404	19881202 <--
AT 120466	E	19950415	AT 1989-900628	19881202 <--
ES 2071681	T3	19950701	ES 1989-900628	19881202 <--
ZA 8809136	A	19890830	ZA 1988-9136	19881206 <--
CA 1339128	A1	19970729	CA 1988-585220	19881207 <--
IL 88629	A1	19940412	IL 1988-88629	19881208 <--
CN 1033458	A	19890621	CN 1988-108277	19881209 <--
US 5376663	A	19941227	US 1989-391538	19890725 <--
NO 8903166	A	19890804	NO 1989-3166	19890804 <--

DK 8903878	A	19890808	DK 1989-3878		19890808 <--
FI 90550	B	19931115	FI 1989-3750		19890809 <--
FI 90550	C	19940225			
PRIORITY APPLN. INFO.:			GB 1987-28820	A	19871209 <--
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			GB 1988-3374	A	19880213 <--
			GB 1988-3375	A	19880213 <--
			GB 1988-3377	A	19880213 <--
			GB 1988-9174	A	19880419 <--
			GB 1988-17624	A	19880723 <--
			GB 1988-18426	A	19880803 <--
			WO 1988-GB1093	A	19881202 <--

OTHER SOURCE(S): MARPAT 113:58793
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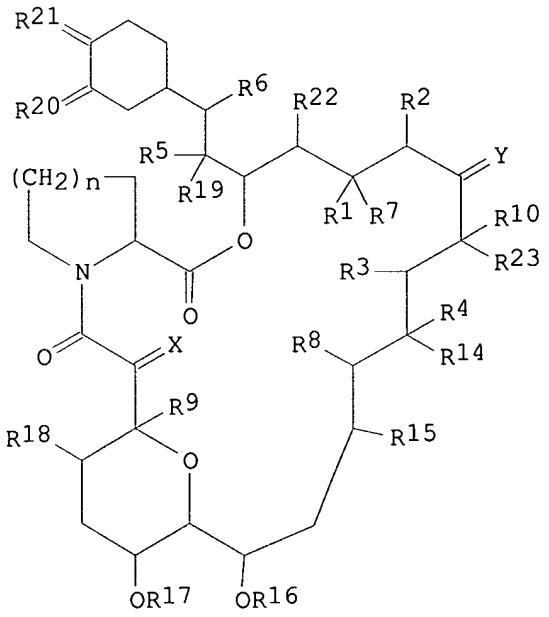


I

AB The title compds. [I; R1R2, R3R4, R5R6 = 2 vicinal H, bond; or R2 = alkyl; R7 = H, OH, alkoxy; or R7R1 = O; R8,R9 = H, OH; R10 = H, (≥1 hydroxy substituted) alkyl or alkenyl, (oxo)alkyl; X = O, (H, OH), (H, H) or CH2O; Y = O, (H, OH), (H, H), NNR11R12, NOR13; R11, R12 = H, alkyl, aryl, tosyl; R13-R19, R22, R23 = H, alkyl; R20, R21 = O, (R24, H), (R25, H); R24, R25 = OH, alkoxy, (OCH2)2CH2OMe; or R24R25 = O in an epoxide ring; n = 1-6; or CY, CR10, or CR23 = 5- or 6-membered N-, S- or O-containing (un)substituted heterocyclyl; with provisos that, e.g. when X = Y = O, then R9 = R25 = OH, R14-R19 = R22 = Me, R24 = MeO, R8 = R23 = H, R3R4 = R5R6 = bond], useful as immunosuppressants, were prepared To a stirred solution of the macrolide FR900506 (200 mg) isolated from Streptomyces (European patent application 0184162) in CH2Cl2 and Et2O was added BF3.Et2O and then a solution of CH2:N2 (600 mg) in Et2O added slowly over 5

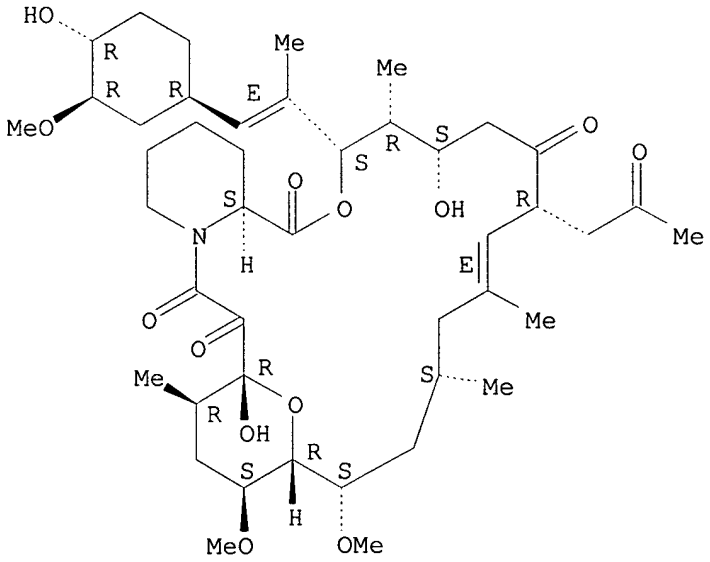
min to give, after purification by silica gel chromatog., 55 mg 17-allyl-1-hydroxy-12-[2-(3,4-dimethoxycyclohexyl)-1-methylvinyl-14,23,25-trimethoxy-13,19,21,27-tetramethyl-11,28-dioxa-4-azatricyclo[22.3.1.04,9]octacos-19-ene-2,3,10,10-tetraone. This inhibited the proliferation of lymphocytes with an IC50 of <1 + 10-6 M.

IT **124554-37-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of, as immunosuppressant)

RN 124554-37-6 HCAPLUS

CN 15,19-Epoxy-3H-pyrido[2,1-c][1,4]oxaazacyclotricosine-1,7,20,21(4H,23H)-tetrone, 5,6,8,11,12,13,14,15,16,17,18,19,24,25,26,26a-hexadecahydro-5,19-dihydroxy-3-[(1E)-2-[(1R,3R,4R)-4-hydroxy-3-methoxycyclohexyl]-1-methylethenyl]-14,16-dimethoxy-4,10,12,18-tetramethyl-8-(2-oxopropyl)-, (3S,4R,5S,8R,9E,12S,14S,15R,16S,18R,19R,26aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



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L10           3 SEA FILE=HCAPLUS ABB=ON  L9 AND (?BRAIN?(W)(?DAMAGE? OR
                ?DISEAS?) OR ?ISCHEM? OR ?HEMORRH? OR ?INFARCT? OR ?INJUR? OR
                ?SUBARACHNOID? OR ?CEREB?(W)?THROMB? OR ?EMBOLISM? OR ?CARDIAC?
                (W)?ARREST? OR ?STROKE? OR ?TRANSIENT?(W)?ISCHEM?(W)?ATTACK?
                OR TIA)
L11       41647 SEA FILE=HCAPLUS ABB=ON  BRAIN DISEASES+ALL/CT
L12           1 SEA FILE=HCAPLUS ABB=ON  L9 AND L11
L13           3 SEA FILE=HCAPLUS ABB=ON  L10 OR L12
L14      144354 SEA FILE=HCAPLUS ABB=ON  ISCHEMIA+ALL/CT
L15           3 SEA FILE=HCAPLUS ABB=ON  L9 AND L14
L19           3 SEA FILE=USPATFULL ABB=ON  L8
L20           2 SEA FILE=USPATFULL ABB=ON  L13 OR L15
L21           3 SEA FILE=USPATFULL ABB=ON  L19 OR L20
L22           1 SEA FILE=USPATFULL ABB=ON  L21 AND (PRD<19990721 OR PD<19990721
                )
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L22  ANSWER 1 OF 1  USPATFULL on STN
ACCESSION NUMBER:        94:113026  USPATFULL
TITLE:                   Macrocyclic compounds
INVENTOR(S):             Cooper, Martin E., Loughborough, England
                         Donald, David K., Ashby de la Zouch, England
                         Hardern, David N., Loughborough, England
PATENT ASSIGNEE(S):      Fisons plc, Ipswich, United Kingdom (non-U.S.
                         corporation)

                              NUMBER        KIND    DATE
                         ---------------- ------ --------
PATENT INFORMATION:      US 5376663               19941227            <--
                         WO 8905304               19890615            <--
APPLICATION INFO.:       US 1989-391538           19890725  (7)
                         WO 1988-GB1093           19881202
                                                  19890725  PCT 371 date
                                                  19890725  PCT 102(e) date

                                NUMBER         DATE
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PRIORITY INFORMATION:    GB 1987-28820       19871209            <--
DOCUMENT TYPE:           Utility
FILE SEGMENT:            Granted
PRIMARY EXAMINER:        Bond, Robert T.
LEGAL REPRESENTATIVE:    McAulay Fisher Nissen Goldberg & Kiel
NUMBER OF CLAIMS:        8
EXEMPLARY CLAIM:         1,8
LINE COUNT:              1094
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB      Compounds of formula (I), in which [R.sup.1 and R.sup.2 ], [R.sup.3 and
        R.sup.4 ] and [R.sup.5 and R.sup.6 ] represent a carbon-carbon bond or
        two hydrogen atoms; R.sup.2 additionally represents alkyl; R.sup.7,
        R.sup.8 and R.sup.9 represent groups including H or OH, R.sup.10 has
        various significances including alkyl and alkenyl; X and Y represent
        groups including O and (H, OH); R.sup.14, R.sup.15, R.sup.16, R.sup.17,
        R.sup.18, R.sup.19, R.sup.22 and R.sup.23 represent H or alkyl; R.sup.20
        and R.sup.21 represent groups including O, (H, OH) and (H, O-alkyl), n
        is 1, 2 or 3, and in addition, Y, R.sup.10 and R.sup.23, together with
        the carbon atoms to which they are attached, may represent a
        heterocyclic ring, (with certain provisos) are described. Processes for
```

making the compounds and pharmaceutical formulations containing them, e.g. for use as immunosuppressive agents, are also described. ##STR1##

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

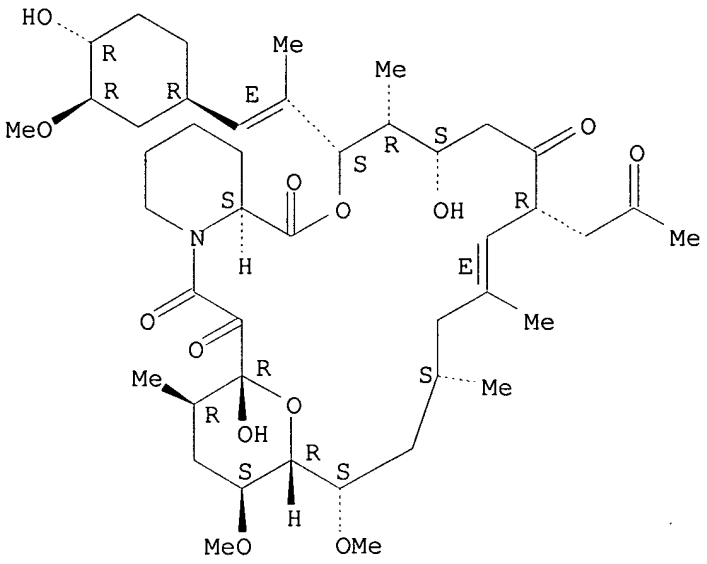
IT **124554-37-6P**

(preparation of, as immunosuppressant)

RN 124554-37-6 USPATFULL

CN 15,19-Epoxy-3H-pyrido[2,1-c][1,4]oxaazacyclotricosine-1,7,20,21(4H,23H)-tetrone, 5,6,8,11,12,13,14,15,16,17,18,19,24,25,26,26a-hexadecahydro-5,19-dihydroxy-3-[(1E)-2-[(1R,3R,4R)-4-hydroxy-3-methoxycyclohexyl]-1-methylethenyl]-14,16-dimethoxy-4,10,12,18-tetramethyl-8-(2-oxopropyl)-, (3S,4R,5S,8R,9E,12S,14S,15R,16S,18R,19R,26aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



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     (FILE 'HOME' ENTERED AT 11:23:58 ON 05 OCT 2005)

     FILE 'HCAPLUS' ENTERED AT 11:24:04 ON 05 OCT 2005
                 E JONES PAUL ALEXANDER/AU
L1            76 SEA ABB=ON  ("JONES PAUL"/AU OR "JONES PAUL A"/AU OR "JONES
                 PAUL ALEXANDER"/AU)
                 E SHARKEY JOHN/AU
L2            59 SEA ABB=ON  ("SHARKEY JOHN"/AU OR "SHARKEY JOHN B"/AU OR
                 "SHARKEY JOHN J"/AU OR "SHARKEY JOHN W"/AU)
                 E KELLY JOHN SHEARER/AU
L3            63 SEA ABB=ON  ("KELLY JOHN S"/AU OR "KELLY JOHN SHEARER"/AU)
L4             2 SEA ABB=ON  L1 AND L2 AND L3
                 SELECT RN L4 1-2

     FILE 'REGISTRY' ENTERED AT 11:25:20 ON 05 OCT 2005
L5             5 SEA ABB=ON  (10102-43-9/BI OR 104987-11-3/BI OR 124554-37-6/BI
                 OR 59865-13-3/BI OR 9025-75-6/BI)

     FILE 'HCAPLUS' ENTERED AT 11:25:25 ON 05 OCT 2005
L6             2 SEA ABB=ON  L4 AND L5
L7               ANALYZE L6 1-2 CT :      11 TERMS

     FILE 'REGISTRY' ENTERED AT 11:30:07 ON 05 OCT 2005
L8             1 SEA ABB=ON  124554-37-6/RN  Segmented compd, located in
                                             Inventor Leach- see orange tag

     FILE 'HCAPLUS' ENTERED AT 11:30:26 ON 05 OCT 2005
L9             7 SEA ABB=ON  L8
L10            3 SEA ABB=ON  L9 AND (?BRAIN?(W)(?DAMAGE? OR ?DISEAS?) OR
                 ?ISCHEM? OR ?HEMORRH? OR ?INFARCT? OR ?INJUR? OR ?SUBARACHNOID?
                  OR ?CEREB?(W)?THROMB? OR ?EMBOLISM? OR ?CARDIAC?(W)?ARREST?
                 OR ?STROKE? OR ?TRANSIENT?(W)?ISCHEM?(W)?ATTACK? OR TIA)
                 E BRAIN DISEASE+ALL
                 E BRAIN DISEASE+ALL/CT
L11        41647 SEA ABB=ON  BRAIN DISEASES+ALL/CT
L12            1 SEA ABB=ON  L9 AND L11
L13            3 SEA ABB=ON  L10 OR L12
L14       144354 SEA ABB=ON  ISCHEMIA+ALL/CT
L15            3 SEA ABB=ON  L9 AND L14
L16            3 SEA ABB=ON  L13 OR L15

     FILE 'MEDLINE, BIOSIS, EMBASE, JAPIO, JICST-EPLUS' ENTERED AT 11:36:16 ON
     05 OCT 2005
L17            0 SEA ABB=ON  L16
L18            0 SEA ABB=ON  L9

     FILE 'USPATFULL' ENTERED AT 11:37:55 ON 05 OCT 2005
L19            3 SEA ABB=ON  L8
L20            2 SEA ABB=ON  L13 OR L15
L21            3 SEA ABB=ON  L19 OR L20
L22            1 SEA ABB=ON  L21 AND (PRD<19990721 OR PD<19990721)  1 cit from
                                                                     US Patfull

     FILE 'HCAPLUS' ENTERED AT 11:38:42 ON 05 OCT 2005
L23            7 SEA ABB=ON  L9 OR L16
L24            3 SEA ABB=ON  L23 AND (PRD<19990721 OR PD<19990721)  3 cits from
                                                                    CA Plus

     FILE HOME

     FILE HCAPLUS
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FILE COVERS 1907 - 5 Oct 2005 VOL 143 ISS 15
FILE LAST UPDATED: 4 Oct 2005 (20051004/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE REGISTRY
Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 4 OCT 2005 HIGHEST RN 864494-87-1
DICTIONARY FILE UPDATES: 4 OCT 2005 HIGHEST RN 864494-87-1

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2005

Please note that search-term pricing does apply when conducting SmartSELECT searches.

****
* *
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added, *
* effective March 20, 2005. A new display format, IDERL, is now *
* available and contains the CA role and document type information. *
* *
****

Structure search iteration limits have been increased. See HELP SLIMITS for details.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/DBSS/registryss.html

FILE MEDLINE
FILE LAST UPDATED: 4 OCT 2005 (20051004/UP). FILE COVERS 1950 TO DATE.

On December 19, 2004, the 2005 MeSH terms were loaded.

The MEDLINE reload for 2005 is now available. For details enter HELP RLOAD at an arrow promt (=>). See also:

http://www.nlm.nih.gov/mesh/
http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html

OLDMEDLINE now back to 1950.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2005 vocabulary.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE BIOSIS
FILE COVERS 1969 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 28 September 2005 (20050928/ED)

FILE RELOADED: 19 October 2003.

FILE EMBASE
FILE COVERS 1974 TO 29 Sep 2005 (20050929/ED)

EMBASE has been reloaded. Enter HELP RLOAD for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE JAPIO
FILE LAST UPDATED: 5 SEP 2005 <20050905/UP>
FILE COVERS APR 1973 TO APRIL 28, 2005

<<< GRAPHIC IMAGES AVAILABLE >>>

FILE JICST-EPLUS
FILE COVERS 1985 TO 3 OCT 2005 (20051003/ED)

THE JICST-EPLUS FILE HAS BEEN RELOADED TO REFLECT THE 1999 CONTROLLED TERM (/CT) THESAURUS RELOAD.

FILE USPATFULL
FILE COVERS 1971 TO PATENT PUBLICATION DATE: 4 Oct 2005 (20051004/PD)
FILE LAST UPDATED: 4 Oct 2005 (20051004/ED)
HIGHEST GRANTED PATENT NUMBER: US6952836
HIGHEST APPLICATION PUBLICATION NUMBER: US2005217002
CA INDEXING IS CURRENT THROUGH 4 Oct 2005 (20051004/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 4 Oct 2005 (20051004/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Aug 2005
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Aug 2005

>>> USPAT2 is now available. USPATFULL contains full text of the <<<
>>> original, i.e., the earliest published granted patents or <<<
>>> applications. USPAT2 contains full text of the latest US <<<
>>> publications, starting in 2001, for the inventions covered in <<<
>>> USPATFULL. A USPATFULL record contains not only the original <<<
>>> published document but also a list of any subsequent <<<
>>> publications. The publication number, patent kind code, and <<<
>>> publication date for all the US publications for an invention <<<
>>> are displayed in the PI (Patent Information) field of USPATFULL <<<
>>> records and may be searched in standard search fields, e.g., /PN, <<<

>>> /PK, etc. <<<

>>> USPATFULL and USPAT2 can be accessed and searched together <<<
>>> through the new cluster USPATALL. Type FILE USPATALL to <<<
>>> enter this cluster. <<<
>>> <<<
>>> Use USPATALL when searching terms such as patent assignees, <<<
>>> classifications, or claims, that may potentially change from <<<
>>> the earliest to the latest publication. <<<

This file contains CAS Registry Numbers for easy and accurate substance identification.

Inventor Search

=> d ibib abs hitstr l6 1-2

L6 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:63812 HCAPLUS
DOCUMENT NUMBER: 134:110473
TITLE: New use of a macrolide tacrolimus analog as a neuroprotectant agent
INVENTOR(S): **Jones, Paul Alexander; Sharkey, John ; Kelly, John Shearer**
PATENT ASSIGNEE(S): Fujisawa Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 9 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001005385	A2	20010125	WO 2000-GB2788	20000719
WO 2001005385	A3	20010802		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2379140	AA	20010125	CA 2000-2379140	20000719
EP 1196170	A2	20020417	EP 2000-946165	20000719
EP 1196170	B1	20040714		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2003504396	T2	20030204	JP 2001-510442	20000719
AT 270888	E	20040715	AT 2000-946165	20000719
PT 1196170	T	20041029	PT 2000-946165	20000719
ES 2220492	T3	20041216	ES 2000-946165	20000719
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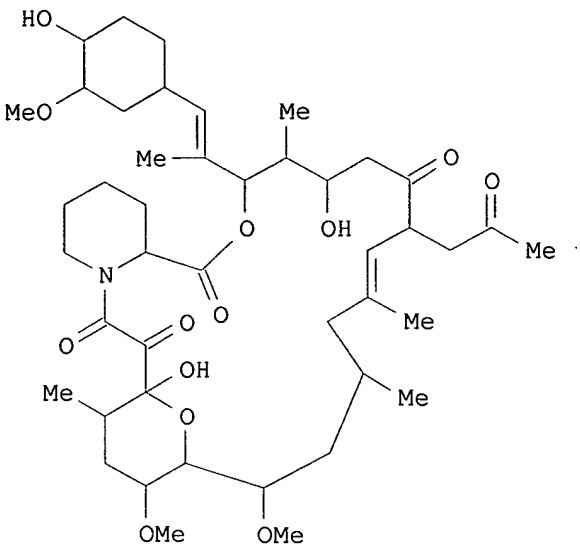
			WO 2000-GB2788	W 20000719

GI



I

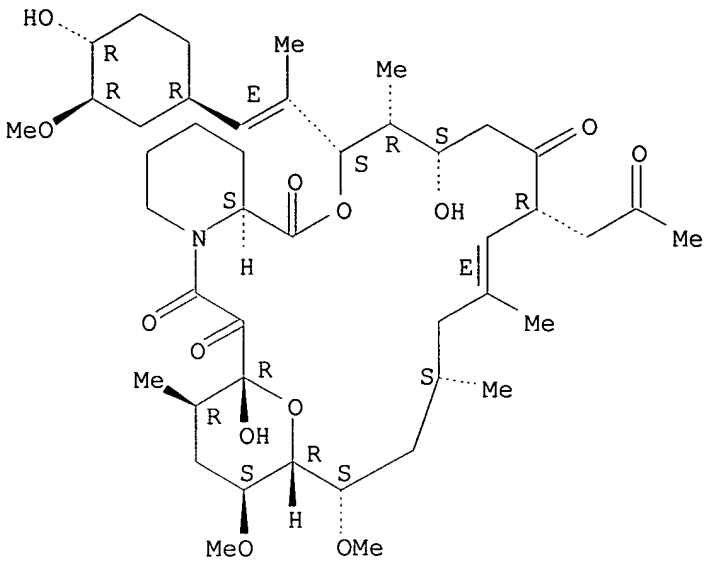
AB A macrolide tacrolimus analog I is provided for use as a neuroprotective agent, particularly for preventing or treating acute or chronic cerebral neurodegenerative diseases.

IT **124554-37-6**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(macrolide tacrolimus analog as neuroprotectant)

RN 124554-37-6 HCAPLUS

CN 15,19-Epoxy-3H-pyrido[2,1-c][1,4]oxaazacyclotricosine-1,7,20,21(4H,23H)-tetrone, 5,6,8,11,12,13,14,15,16,17,18,19,24,25,26,26a-hexadecahydro-5,19-dihydroxy-3-[(1E)-2-[(1R,3R,4R)-4-hydroxy-3-methoxycyclohexyl]-1-methylethenyl]-14,16-dimethoxy-4,10,12,18-tetramethyl-8-(2-oxopropyl)-, (3S,4R,5S,8R,9E,12S,14S,15R,16S,18R,19R,26aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



L6 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:92736 HCAPLUS
DOCUMENT NUMBER: 133:48
TITLE: Calcineurin inhibitors as neuroprotectants: focus of tacrolimus and cyclosporin
AUTHOR(S): **Sharkey, John; Jones, Paul A.**; McCarter, Jennifer F.; **Kelly, John S.**
CORPORATE SOURCE: University Department of Neuroscience, Fujisawa Institute of Neuroscience, Edinburgh, UK
SOURCE: CNS Drugs (2000), 13(1), 1-13
CODEN: CNDREF; ISSN: 1172-7047
PUBLISHER: Adis International Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 207 refs. Tacrolimus (FK506) and cyclosporin (cyclosporin-A) are potent immunosuppressants which are presently in clin. use for the treatment of allograft rejection. Recent studies suggest that tacrolimus and cyclosporin may also be of therapeutic benefit for the treatment of neurodegenerative disorders, in particular those associated with acute brain ischemia. At immunosuppressive doses, tacrolimus is a powerful neuroprotectant in many exptl. models of cerebral ischemia: reducing infarct volume and improving neurol. outcome. In rat focal ischemia models neuroprotection can be elicited by a single injection of tacrolimus given up to 72 h before or up to 2 h after the insult. A similar postocclusion window of efficacy has been reported in the gerbil forebrain ischemia model. These neuroprotective properties are also shared by cyclosporin, although the poor penetration of cyclosporin across the blood-brain barrier necessitates the use of high doses (20 mg/kg) of this drug to achieve neuroprotection. The observation that sirolimus (rapamycin) is not neuroprotective in models of focal cerebral ischemia, but can effectively inhibit the neuroprotective effects of tacrolimus, supports the view that the protective effects of tacrolimus are mediated via the inhibition of calcineurin.

IT **9025-75-6**, Calcineurin **10102-43-9**, Nitric oxide, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)

(calcineurin inhibitors as neuroprotectants: focus of tacrolimus and cyclosporin)
RN 9025-75-6 HCAPLUS
CN Phosphatase, protein phosphoserine/phosphothreonine (9CI) (CA INDEX NAME)

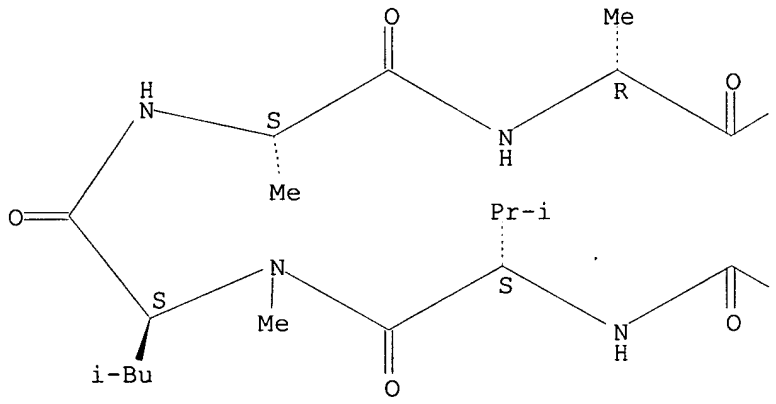
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 10102-43-9 HCAPLUS
CN Nitrogen oxide (NO) (8CI, 9CI) (CA INDEX NAME)

N═O

IT **59865-13-3**, Cyclosporin a **104987-11-3**, Tacrolimus
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(calcineurin inhibitors as neuroprotectants: focus of tacrolimus and cyclosporin)
RN 59865-13-3 HCAPLUS
CN Cyclosporin A (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



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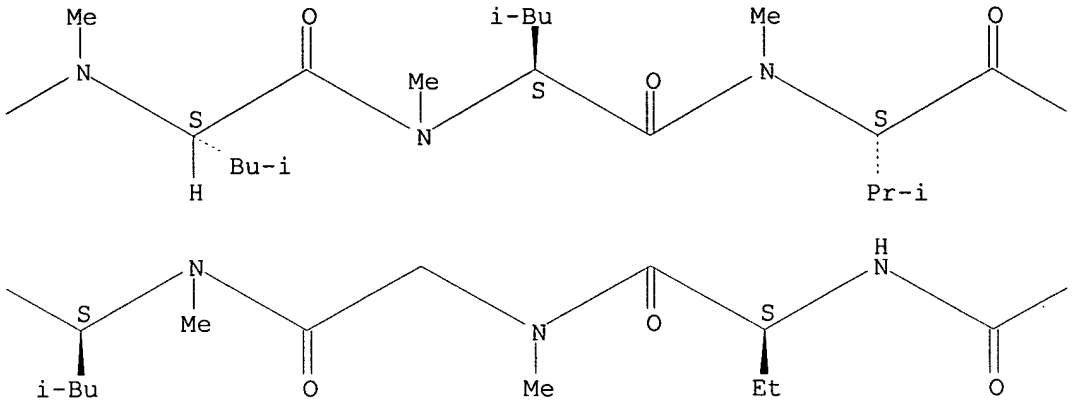

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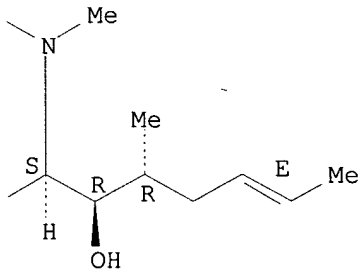
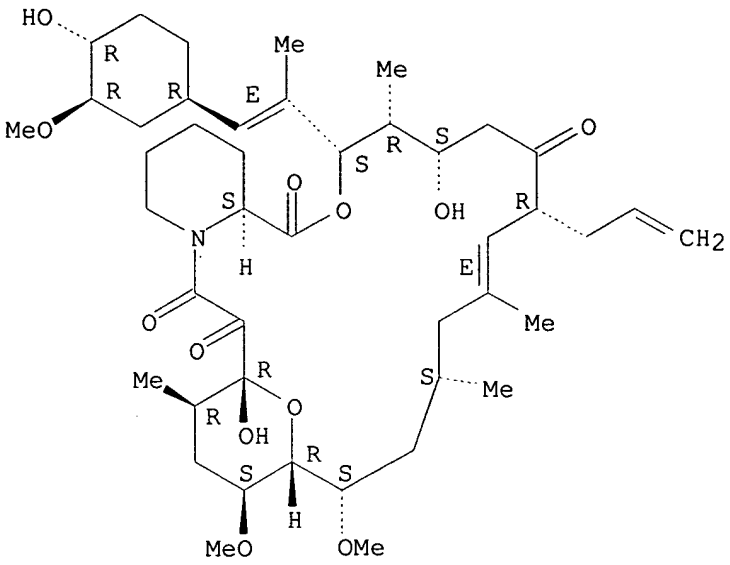


RN 104987-11-3 HCAPLUS
CN 15,19-Epoxy-3H-pyrido[2,1-c][1,4]oxaazacyclotricosine-1,7,20,21(4H,23H)-tetrone, 5,6,8,11,12,13,14,15,16,17,18,19,24,25,26,26a-hexadecahydro-5,19-dihydroxy-3-[(1E)-2-[(1R,3R,4R)-4-hydroxy-3-methoxycyclohexyl]-1-methylethenyl]-14,16-dimethoxy-4,10,12,18-tetramethyl-8-(2-propenyl)-, (3S,4R,5S,8R,9E,12S,14S,15R,16S,18R,19R,26aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



REFERENCE COUNT: 207 THERE ARE 207 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT